IN THE U.S. PATENT AND TRADEMARK OFFICE

Applicant: Jong Soo WOO
Serial No.: 10/762,239 Art Unit: 1615 Filed: January 23, 2004
Examiner: Retford Berko
For: Enteric Coated Formulation of a Benzimidazole Derivative And Method of Preparation Thereof

DECLARATION UNDER 37 C.F.R. SECTION 1.132

Commissioner for Patents
Alexandria, VA 22314-1450

I, Jong Soo WOO, a citizen of Korea, residing at Daelim-Jinheong Apt. #821-105, Daewol-Maeul, 914, Jungia-Dong, Jangan-Ku, Suwon-Shi, Kyunggi-Do, Korea, hereby declares as follows:

1. I am an inventor of the subject matter of the above identified application.

2. My personal particulars are summarized as follows:

[Education]
1998. 3 – 2001. 2: Ph.D. (pharmaceutics) College of Pharmacy, Chungnam National University
1996. 3 - 1998. 2: M.S. (Pharmaceutics), College of Pharmacy, Chungnam National University
1986. 3 - 1990. 2: B.S. (Pharmaceutics), College of Pharmacy, Youngnam University

[Employment]
1990. 2 - 1992. 1: Researcher, Department of Quality Control, Hanmi Pharm Company
1992. 2 - 1999. 3: Chief Researcher, Pharmaceutical Research Center, Hanmi Pharm Company
1999. 4 - 2003. 12: Team Leader, Pharmaceutical Research Team, Hanmi Pharm Company
2004. 1 – Present : Director, Pharmaceutical Research Center, Hanmi Pharm Company
2003. 1 – Present : Professor, College of Pharmacy, Youngnam University

[Publications]
Jong Soo Woo et al., Enhanced Oral Bioavailability of Paclitaxel by Coadministration of the P-Glycoprotein Inhibitor KR30031. Pharmaceutical Research, 20(1), 24-30, 2003.

Jong Soo Woo et al., HPLC of Acetyl-L-carnitine in Human Plasma by Derivatization with

p-Bromophenacyl Bromide. I: *Liq. Chrom. & Rel. Techno/.*, 24(4), 555-563, 2001.

Jong Soo Woo et al., Preparation and Evaluation of Non-crystalline Cefuroxime Axetil Solid Dispersion. I: *Kor. Pharm. Sci.*, 32(2), 73-80, 2002.

Jong Soo Woo et al., Bioequivalence ofHanmi Domperidone Tablets to Motilium-M Tablets (Domperidone Maleate 12.72mg). I: *Pharm. Sci. (C.N. U).* 17, 96-105, 2002.

Jong Soo Woo et al., Preparation and Evaluation of Bupivacaine Microspheres by a Solvent Evaporation Method (II). *Yakhak Hoeji.* 45(6),623-633, 2001.

Jong Soo Woo et al., Bioequivalence Study of Acetyl-L-Carnitine Tablets. *The Journalof Applied Pharmacology,* 9(4),285-290, 2001.

[Patent Applications]
Since 1996, I have filed about 40 patent applications related to cyclosporin and omeprazole in the Patent Offices in the world including Korea, U.S.A., Europe, Japan etc., some of which were issued in Korea (Patent Nos. 150830,167613, 137696, 183449, 135736, 216623) and in U.S.A.(Patent Nos. 5639474, 5589455, 5603951, 6039981, 6017290) and so on.

3. I am thoroughly familiar with the Office Action dated September 16, 2004, wherein claims 1,2,8,9 and 10 of the present application are rejected under 35 U.S.C. 103(a) as being unpatentable over Lovgren et al (US 4,786,505) in view of Makino et al (US 5,026,560) further in view of Sarett et al (US 3,336,192), or over Lovgren et a. (US 4,786,505) in view of Chen et al (US 6,726,927) further in view of Pierre et al (US 3,324,102).

4. Under my direction and control, a series of accelerated stability tests were conducted for i) comparison of omeprazole formulation using HP-50 and HP-55; and ii) comparison of pantoprazole formulation using HP-50 and HP-55.

(1) Preparation of Test Samples

Fifteen core tablets per sample having the ingredients as shown in the following Table 1 were prepared in accordance with the same procedure as Example 1 of the present specification.

Table 1. Composition for core tablets

Ingredients (mg)	Sample 1	Sample 2	Sample 3	Sample 4
Omeprazole-cholestyramine complex	40	40	-	-
Pantoprazole- cholestyramine complex	-	-	40	40
Hydroxypropyl cellulose-L	45	45	45	45
Lactose for direct method (Ludipress, BASF)	193	193	193	193
Sodium starch glycolate	21.2	21.2	21.2	21.2
Silicon dioxide	0.8	0.8	0.8	0.8
Magnesium stearate	2	2	2	2

The obtained core tablets were coated in a pan with the coating compositions which have the ingredients as shown in the following Table 2.

Table 2. Coating composition

Ingredients (mg)	Sample 1	Sample 2	Sample 3	Sample 4
Hydroxyproply methylcellulose phthalate HP-50	40		40	-
Hydroxyproply methylcellulose phthalate HP-55	-	40	-	40
Myvacet	2	2	2	2
Acetone	360	360	360	360
95% Ethanol	180	180	180	180

(2) Test Method

Respective samples were kept under accelerated condition [40 °C, relative humidity (RH) of 75%] for six months. Changes of the residual contents according to the lapse of time in samples were compared after 0, 1, 2, 4, and 6 month(s) (the comparative tests of the contents are based on Test Example 2 of the present specification).

Column; μ -Bondapak C18
Detection; UV 280 nm
Mobile phase; acetonitrile; phosphate buffer at pH 7.6 = 34:66
Injection volume; 10 μ l
Flow rate; 1.1 ml/min

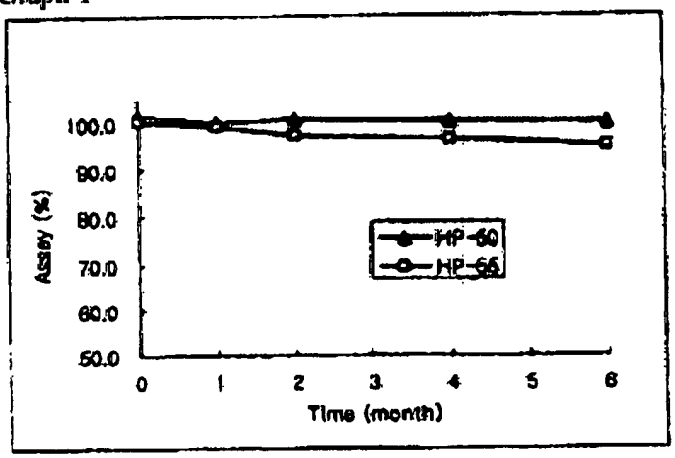
(3) Test Results (Residual Content)

1) The results of the accelerated stability tests of omeprazole formulations according to the kinds of enteric coating (HP-50, HP-55) are shown in Table 3 and Graph I below.

Table 3.

	At First	After 1 month	After 2 months	After 4 Months	After 6 months
Sample 1	101.5	100.2	100.7	100.3	100.1
Sample 2	100.3	99.2	97.5	96.5	95.0

Graph 1



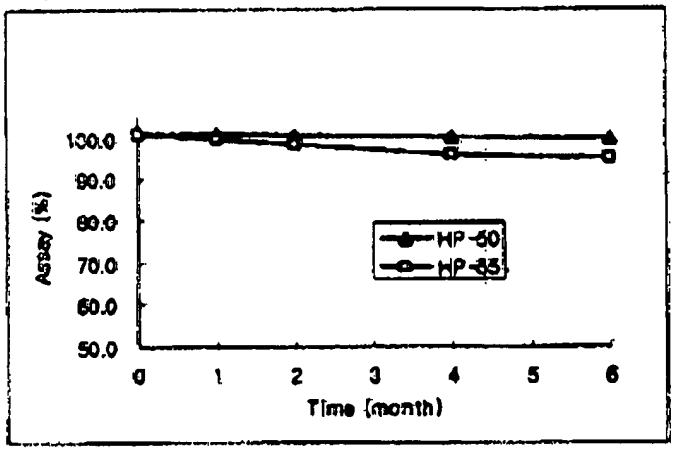
2) The results of the accelerated stability tests of pantoprazole formulation according to the kinds of enteric coating (HP-50, HP-55) are shown in Table 4 and Graph 2 below.

Table 4.

	At First	After 1 month	After 2 months	After 4 Months	After 6 months
Sample 4	101.0	101.2	100.8	100.4	100.1

Sample 5	101.0	100.1	98.5	96.3	95.2

Graph 2



(4) Conclusion

1) Accelerated stability test of omeprazole formulation according to the kinds of enteric coating (HP-50, HP-55)

From the results in the above Table 3 and Graph 1, it can be seen that omeprazole formulation coated with HP-50 (Sample 1) has a higher residual content than omeprazole formulation coated with HP-55 (Sample 2) in the accelerated tests for 6 months.

2) Accelerated stability test of pantoprazole formulation according to the kinds of enteric coating (HP-50, HP-55)

From the results in the above Table 4 and Graph 2, it can be seen that pantoprazole formulation coated with HP-50 (Sample 3) has a higher residual content than omeprazole formulation coated with HP-55 (Sample 4) in the accelerated tests for 6 months.

5. I hereby declare that all statements made herein to our own knowledge are true and statement made on information and belief are believed to be true; further that these statements

were made with the knowledge that willful false statement and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code that such willful false statement may jeopardize that validity of the application or any patents issuing thereon.

Dated February 11 2005

Signature: J. S. Woo

Jong Soo WOO

(4号)

Shin-Etsu

2002/06/18 (1/1)

Certificate of Analysis

Shin-Etsu Chemical Co., Ltd.
Naoetsu Plant Quality Assurance Depar
28-1 Nishifukushima, Kubiki-mura,
Nakakubiki-gun, Niigata, Japan

Product Name	HPMCP (Hypromellose Phthalate, NF)
Grade	HP-50
Nominal Phthalyl Content	24 %
Viscosity Type	55 cSt
Lot Number	202114
Quantity	25kg
Manufacture Date	2002/02/25
Expiration Date	2005/02/24
Analysis Date	2002/02/27
Issue No.	06120020601086002-1-01
Remark	

This material does not require OVI testing, under the USP-NF <467> stipulation that "… based on knowledge of the manufacturing process and controlled handling and storage… there is no potential for the specific toxic solvents to be present … if tested, will comply with established standards."
This product complies with the specifications described in the current NF, EP and JP.
This product is manufactured in accordance with GMP.

Test Item	Unit	Test Result	Specification
Appearance		White Powder or Granules	
Identification		Conforms	Conforms
Viscosity	cSt	57.6	44 - 66
Water	%	0.6	6.0 Max.
Residue on Ignition	%	0.02	0.20 Max.
Chloride	%	Not more than 0.07	Not more than 0.07
Heavy Metals	%	Not more than 0.001	Not more than 0.001
Limit of Free Phthalic Acid	%	0.13	1.0 Max.
Phtalyl Content	%	22.7	21.0 - 27.0
Methoxyl Content	%	22.2	20.0 - 24.0
Hydroxypropoxyl Content	%	7.2	6.0 - 10.0

K. Araume

KIYOSHI ARAUME
General Manager, Q. A. Dept.

Shin-Etsu No. : 12009105-10-01

Issue:
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Shin-Etsu

2002/12/18 (1/1)

Certificate of Analysis

Shin-Etsu Chemical Co., Ltd.
Naoetsu Plant Quality Assurance Department
28-1 Nishifukushima, Kubiki-mura,
Nakakubiki-gun, Niigata, Japan

Product Name	HPMCP (Hypromellose Phthalate, NF)
Grade	HP-55
Nominal Phthalyl Content	31 %
Viscosity Type	40 cSt
Lot Number	211442
Quantity	600kg
Manufacture Date	2002/11/30
Expiration Date	2005/11/29
Analysis Date	2002/12/03
Issue No.	D5120021201451002-1-01

Remark
This material does not require OVI testing, under the USP-NF <467> stipulation that "… based on knowledge of the manufacturing process and controlled handling and storage… there is no potential for the specific toxic solvents to be present … If tested, will comply with established standards."
This product complies with the specifications described in the current NF, EP and JP.
This product is manufactured in accordance with GMP.

Test Item	Unit	Test Result	Specification
Appearance		White Powder or Granules	
Identification		Conforms	Conforms
Viscosity	cSt	42.8	32 - 48
Water	%	1.0	5.0 Max.
Residue on Ignition	%	0.02	0.20 Max.
Chloride	%	Not more than 0.07	Not more than 0.07
Heavy Metals	%	Not more than 0.001	Not more than 0.001
Limit of Free Phthalic Acid	%	0.18	1.0 Max.
Phthalyl Content	%	33.3	27.0 - 35.0
Methoxyl Content	%	19.4	18.0 - 22.0
Hydroxypropoxyl Content	%	6.1	5.0 - 9.0

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